UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,976	02/02/2006	Anders Per Sorensen	HOI-14402/16	5610

25006 7590 07/03/2008

GIFFORD, KRASS, SPRINKLE,ANDERSON & CITKOWSKI, P.C
PO BOX 7021
TROY, MI 48007-7021

EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
07/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,976	SORENSEN ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,17,18 and 20-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,17,18 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 14, 2008 has been entered.

Accordingly, claims 1-11, 17-18, and 20-30 are pending in the instant application.

Claim Rejections - 35 USC § 112

1. The rejection of claims 1-11, 17-18, and 20-30 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants are asserting that patent claims are enabled so long as they do not require experimentation to practice them. Applicants further assert that a person of ordinary skill in the art would not have to predict which substitutions would result in an antibody capable of specifically binding PsaA protein, instead the skill artisan would be able to employ the disclosed and other routine methods that are described in the specification or are otherwise known in the art to identify substitutions of the disclosed

sequences that fall within the scope of the claims.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants assert that the claims are enabled so long as they do not require experimentation to practice them. Presumably, Applicants intended to assert that the claims to not require undue experimentation. However, Applicants are respectfully directed back to their own claim language. Claim 1 recites an isolated binding polypeptide comprising at least a first and a second binding domain, wherein the first domain comprises SEQ ID NO: 6 or ***a variant of SEQ ID NO: 6 having a single amino acid substitution***. (Empasis added). Given that SEQ ID NO: 6 is 9 amino acids long and that there are twenty naturally occurring amino acids, this creates $(20)^9$ possible variants of SEQ ID NO: 6. Doing the math this generates 512,000,000,000 distinct variants for SEQ ID NO: 6 alone. This does not even evaluate the further variants allowed to the second binding domain, SEQ ID NO: 4. The CDR identified as SEQ ID NO: 4 contains 7 amino acids, or another $(20)^7$ possible variants in addition to the $(20)^9$ variants already created by the first binding domain. Combined the two variants generate a staggering 655,360,000,000,000,000,000 possible variants, a number the Examiner is not even sure how to name. Furthermore, the resulting variants create a scenario in which only two binding domains are present, as previously set forth by Padlan et al in which all 6 CDRs contribute at least one residue to binding and one residue in the framework is also in contact with the antigen. Simply recited, the generation of 655,360,000,000,000,000,000 variants, which are themselves only partial

structures of an antibody, rises to the level of undue experimentation for generating polypeptides which bind to Streptococcus pneumoniae surface adhesin A.

Padlan et al (PNAS (1989) 86:5938-5942) describe the crystal structure of an antibody-lysozyme complex where all 6 CDRs contribute at least one residue to binding and one residue in the framework is also in contact with the antigen.

Vajdos et al (J. Mol. Biol. (2002) 320 : 415-428) set forth that antigen binding is primarily mediated by the CDRs but more highly conserved framework segments are mainly involved in supporting CDR loop conformations and in some cases framework residues also contact antigen.

MacCallum et al (J. Mol. Biol. (1996) 262 : 732-745) analyzed many different antibodies for interaction with antigen and found that although CDR3 of the VH dominate the interaction, a number of residues outside the CDRs make antigen contacts and residues in the CDRs are important for backbone conformations.

De Pascalis et al (Journal of Immunology 2002 169: 3076-3084) teach that grafting of CDRs onto a human framework required some residues in all 6 CDRs as well as specific frameworks.

As demonstrated by the cited references above, it is unpredictable which amino acids could be removed, added or substituted, as often all 6 CDRs and even framework regions of an antibody contribute to antigen binding.

The instant claims are drawn to binding polypeptides comprising a sequence or "variant having a single amino acid substitution" thereof. Selective point mutations to

one key residue could eliminate the function of the polypeptide. It could eliminate its binding properties. If the range of decreased binding ability after single point mutations of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of function, depending on the relative importance to the binding interaction of the altered residue. As stated above, Applicants have not shown which amino acids may be changed without causing a detrimental effect to the binding domain in which it represents. The claims allow for as many as 655,360,000,000,000,000,000 variants, e.g., variants of SEQ ID NO: 4 or 6 having a single amino acid substitution. Applicants have provided no guidance to enable one of skill in the art how to determine without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made.

"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that a "patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.)" Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Given the lack of guidance contained in the specification regarding acceptable amino acid substitutions, additions or deletions, one of skill in the art would be forced into excessive experimentation to

practice the broadly claimed invention.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

2. The rejection of claims 1-11, 17-18 and 20-30 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicants are asserting that Example 14 of the Synopsis of Application of Written Description Guidelines issued by the US Patent Office clearly states that protein variants can meet the requirements of 35 USC 112, first paragraph.

Applicants arguments have been fully considered but are not found to be persuasive.

First, Applicants reference to Example 14 is outdated, the new written description guidelines have replaced Applicants Example 14. Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, the guidelines can be found at the following link on the USPTO Internet in "Patents Guidance" Specifically, Example 10, which is analogous to the recitation of claiming a product (binding polypeptide) based on a particular function (binding Streptococcus pneumoniae surface adhesion A). <http://www.uspto.gov/web/patents/guides.htm>

Although the disclosure of SEQ ID NO: 4 and 6 puts one of ordinary skill in the art of possession of variants of SEQ ID NO: 4 and 6 having a single amino acid substitution, the level of ordinary skill in the art is such that one of ordinary skill would

not be able to identify without further testing which of those proteins having an amino acid substitution in SEQ ID NO: 4 or 6 when combined with further unidentified CDRs retain the activity of specifically binding Streptococcus pneumoniae surface adhesion A. Based on the lack of knowledge and the unpredictability in the art, those of ordinary skill in the art would not conclude that the Applicants was in possession of the claimed genus of proteins based on the single disclosed species of SEQ ID NO 4 in combination with SEQ ID NO: 6.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts*., 18 USPQ2d 1016.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43

USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The rejection of claims 1-5, 10-11, 14, 17-18, and 20-23 under 35 U.S.C. 102(b) as being anticipated by Korman et al in light of Hoogenboom is withdrawn in view of

Applicants amendment.

4. The rejection of claims 1-7, and 17 under 35 U.S.C. 102(b) as being anticipated by Crook et al in light of Hoogenboom is withdrawn in view of Applicants amendment.

5. The rejection of claims 1-7, 10, and 22 under 35 U.S.C. 102(b) as being anticipated by Srivastava et al in light of Hoogenboom is withdrawn in view of Applicants amendment.

6. The rejection of claims 6, 7, 24, 29 and 30 under 35 U.S.C. 102(b) as being anticipated by Gor et al in light of Hoogenboom is withdrawn in view of Applicants amendment.

Claim Rejections - 35 USC § 103

7. The rejection of claims 6-9, 20-21 and 23 under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al or Korman et al in view of Kriangkum et al and Hoogenboom is withdrawn in view of Applicants amendment.

Claim Objections

8. The objection of claim 14 is withdrawn in view of the cancellation of said claim.

The following new grounds of rejection are applied to the claims:

Claim Rejections - 35 USC § 112

9. Claims 1-11, 17-18, and 20-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants have amended claim 1 to recite "having a single amino acid substitution." Applicants assert that support is found at lines 20-33 of the specification. The Examiner can only assume that Applicants are referring to page 1, lines 20-33, however this section of the specification provides zero guidance relating to a "single amino acid substitution." Applicants are required to demonstrate clear support (page and line number of the specification) for the newly added limitation, or cancel the newly added limitation.

All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shannon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
June 30, 2008